

RECORD OF ORAL HEARING
UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Administrative Patent Judge Sally Gardner Lane

JEAN-LOUIS RUELLE
Junior Party
(Patent 6,780,419
Application No. 10/896,778),

v.

VINCENZO SCARLATO, VEGA MASIGNANI, RINO RAPPUOLI,
MARIAGRAZIA PIZZA, and GUIDO GRANDI
Senior Party
(U.S. Application 11/212,443).

Patent Interference No. 105,551

Oral Hearing Held: April 15, 2010

Before SALLY G. LANE, RICHARD E. SCHAFER and MICHAEL P.
TIERNEY, *Administrative Patent Judges.*

1 APPEARANCES:

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P R O C E E D I N G S

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2 JUDGE LANE: We're here for oral argument in interference
3 105,551, Ruelle v. Scarlato, and we'll start with Junior Party. Mr. Olstein,
4 can you tell us who you have with you?

5 MR. OLSTEIN: Yes. Elliot Olstein representing the Junior Party.
6 Mr. Lillie of my firm is also present as counsel. And from the Client, GSK,
7 Alice Bradney and Michael Leanski (ph.).

8 JUDGE LANE: All right. Mr. Kreeger?

9 MR. KREEGER: Good afternoon, Your Honor. Matthew Kreeger
10 from Morrison & Foerster. With me from my firm is Otis Littlefield.

11 JUDGE LANE: Thank you. Okay. I think in the order it said each
12 side would have 20 minutes, right? So we'll start with Junior Party, and,
13 Mr. Olstein you can reserve appropriate time for rebuttal, if you'd like.

14 MR. OLSTEIN: Your Honor, I will be proceeding one motion at a
15 time, as we did in the previous proceedings; that first we would argue the
16 Ruelle priority motions, then after that, follow that by arguing --

17 JUDGE LANE: Well, you would reserve time for your rebuttal if you
18 want to rebut, I suppose, the Scarlato priority case. So you're going to argue
19 your priority case at this time.

20 MR. OLSTEIN: Just my priority case?

21 JUDGE LANE: Yes.

22 MR. OLSTEIN: Thank you, Your Honors. For the --

23 JUDGE LANE: I'm sorry --

24 MR. OLSTEIN: Okay. I just wanted to be sure we're set.

25 JUDGE LANE: Okay. I'm sorry.

26 MR. OLSTEIN: No, it's fine. For the Ruelle priority case --

1 JUDGE LANE: Do you want to save some time? How do you want
2 to split up your time?

3 MR. OLSTEIN: Well, I would like to save time, but may I just have a
4 little clarification? I'm going to present my priority case first. Mr. Kreeger
5 is going to then answer my priority case, and then present his priority case?

6 JUDGE LANE: Right. And then any -- yes, and then he can reserve
7 a little time for something that he may have in reply.

8 MR. OLSTEIN: Then I can rebut?

9 JUDGE LANE: Well, no, we're not going to go on and on, but --

10 JUDGE SCHAFER: Two and two?

11 JUDGE LANE: Yeah, two and two. Thank you.

12 JUDGE SCHAFER: You get a chance to present your case.

13 MR. OLSTEIN: Yes.

14 JUDGE SCHAFER: Then they'll present theirs. Then you'll get a
15 chance to rebut, and then he'll get a chance to rebut. So it's just -- both of
16 you will get -- since you both have motions, you'll each get an opportunity to
17 present your case and a rebuttal.

18 JUDGE LANE: Is your confusion that you don't know whether you
19 should speak about your opposition in the first part of your argument?

20 MR. OLSTEIN: Well, yes, because the last time when we proceeded,
21 we took one motion at a time.

22 JUDGE LANE: Oh, when we were doing nonpriority motions?

23 MR. OLSTEIN: Yeah. And what we did is the Junior Party
24 presented his motions in toto, then there was a reply, and then there was a
25 rebuttal, and then the Senior Party -- and that's -- I'll do it any way Your
26

1 Honors would like us to do it. I'm just trying to find out what is the
2 procedure so I know how to reserve.

3 JUDGE LANE: Okay. Well, let's do it this way: Let's hear your
4 priority case, and then we'll give you some time in rebuttal. I just wanted to
5 kind of see how much time you wanted for each portion of your argument.

6 MR. OLSTEIN: Okay. Well, --

7 JUDGE LANE: What do you think?

8 MR. OLSTEIN: If I get 20 minutes, I will take -- approximately split
9 it in half.

10 JUDGE LANE: All right.

11 MR. OLSTEIN: Maybe reserve a little --

12 JUDGE LANE: We may have a lot of questions, anyway.

13 MR. OLSTEIN: Yeah.

14 JUDGE LANE: Continue.

15 MR. OLSTEIN: So in any event, in the Ruelle priority case, there are
16 really only two issues that are before this Board. Conception has been
17 conceded, so the issues that are left is whether or not -- and our February
18 reduction to practice has also been conceded. So the two issues in this is
19 what I call our first or initial reduction to practice and diligence. For our
20 initial reduction to practice, we rely on work that was performed prior to the
21 constructive filing date of the Scarlato priority case, but because of the
22 statements that were put in, even if we prove that case, we will only get a
23 date after his priority filing, which would be -- his priority filing was
24 January 14th, and we would get January 16th.

25 So with respect to the first reduction of practice, Dr. Pullen, who
26 performed the work on behalf of Inventor Ruelle, testified that he

1 understood and believed he had produced a polypeptide within the count in
2 December 1997.

3 JUDGE SCHAFER: Tell me what that means, within the count,
4 because I look at the count, you have a full -- there's a full amino acid
5 sequence, and then there's this 15 contiguous amino acids. Which --

6 MR. OLSTEIN: Well, he produced a fragment of the entire sequence.

7 JUDGE SCHAFER: So you're focusing on one of the -- that you had
8 15 --

9 MR. OLSTEIN: Part B of the count.

10 JUDGE SCHAFER: Yeah, 15 contiguous amino acids.

11 MR. OLSTEIN: Correct, Your Honor.

12 JUDGE SCHAFER: Of the particular sequence.

13 MR. OLSTEIN: Yes.

14 JUDGE SCHAFER: Okay.

15 JUDGE LANE: Mr. Olstein, when I was first reading your Brief, it
16 seemed to me like you were saying that they had taken this vector and put it
17 into the E. coli cells, and then they kept them at a certain temperature so as
18 not to express the protein. So now you're -- in this December work. So is
19 that what happened? I mean, how did they -- it seemed more, maybe, in
20 your Reply you talked about this leaky thing. So I was trying to figure out
21 where you talk about, in your Initial Brief, where they actually express the
22 protein.

23 MR. OLSTEIN: Well, it's in the Initial Brief and it's in Dr. Pullen's
24 Declaration, initially. His paragraphs 48, 55 to 60, 70 and 80 explain that he
25 did understand that he had expressed polypeptide as of that December '97
26 date. And because of the fact that there was an inhibitor in there, normally,

1 these inhibitors are supposed to express only when you elevate temperature.
2 But Dr. Pullen had a lot of experience with this particular type of expression
3 system, and based on that experience, he knew that even though you only
4 maintained it at 30 degrees C, so-called leakiness. In other words, there
5 would be expression. So he prepared a vector for the express purpose of
6 expressing the polypeptide of the count. He had --

7 JUDGE LANE: So let me get back to that. So it's like an incidental
8 expression? Because it seemed to me like he didn't intend to express it, he
9 intended to not express it by keeping it at the certain temperature.

10 MR. OLSTEIN: Well, he inherited a vector system, okay, that he had
11 experience with. That vector system did have the inhibitor, and the intent of
12 whoever initially developed that vector system would have been so as to
13 express only at 39 degrees C. But what he testified was that he had
14 previously used that same type of expression system that had that same type
15 of inhibitor, and he knew that even if he was at 30 degrees C, he would be
16 getting expression because of his prior experience with that particular
17 system.

18 JUDGE LANE: Did he actually do some sort of a test to confirm that
19 he did get protein?

20 MR. OLSTEIN: He did not do a test at that time to confirm that the
21 protein -- but based on the fact that this was a well-known expression system
22 and that he had used it numerous times in the past, he knew that at 30
23 degrees C, he would get expression from that system. And what he had
24 done was test the actual vector to make sure that he had the DNA in the
25 vector. He had tested the E. coli cells to make sure that the vector was in the
26 E. coli cells. And based on his prior experience knowing how the biological

1 systems work and they normally express protein once you have it in the
2 correct orientation, and once you know that it is in the E. coli, and once he
3 knew that this type of expression system would express at 30 degrees C, his
4 testimony was that he knew and understood at the time that he had expressed
5 polypeptide --

6 JUDGE SCHAFER: Well, what you're saying is he has a belief that it
7 was there. Can you cite a case that says, for an actual reduction to practice,
8 the person doing the test, his belief that he got some is sufficient as opposed
9 to actual proof that he actually got the stuff?

10 MR. OLSTEIN: Well, what we have done is produce evidence to
11 show that it did in fact express at that time, although that was subsequent
12 evidence to confirm. This is confirming evidence that it actually did work,
13 because that set of cells --

14 JUDGE SCHAFER: So you did -- so you subsequently did the same
15 thing? You took the same vector, the same critter with the vector and -- at
16 30 degrees and then tested what you got, and you ended up showing that the
17 protein was there?

18 MR. OLSTEIN: Yeah. Not to mislead, Your Honor; that
19 confirmatory test was not a contemporaneous test.

20 JUDGE SCHAFER: Right. I understand.

21 MR. OLSTEIN: It was done in 2009.

22 JUDGE SCHAFER: Yeah, there's plenty of case law that says you
23 can test something later to show that you had some property of a compound
24 or something. But that's what your case is, actually, is that here's what we
25 did at the time, the person who did the test believed they had it, and then

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1 subsequent tests under that condition show that his belief was in fact
2 correct?

3 MR. OLSTEIN: That is correct, Your Honor.

4 JUDGE SCHAFER: Okay.

5 MR. OLSTEIN: And what we have done was place into evidence,
6 confirmatory as we call it, that 2009 test, and we also placed into evidence
7 his experience and his knowledge that this was leaking, as Judge Lane called
8 it, and as we call it, in fact did produce -- there was literature
9 contemporaneous. Not that he knew of it at the time, but just as
10 confirmatory evidence to indicate that it was already known in the art that
11 this type of promoter system did leak, even when at 30 degrees C. So it's
12 confirmatory evidence to support the credibility of his testimony as opposed
13 to providing evidence that he knew and believed it. And, Your Honors, I
14 want to point out that at no time in this case, although Scarlato had ample
15 opportunity, did they provide any evidence, any expert testimony, any
16 cross-examination testimony that challenged the tests that were done in
17 2009, challenged or indicated that this promoter was not a leaky system, no
18 evidence to that effect, challenged -- they had opportunity to cross-examine
19 Dr. Puller that in fact he had this belief and this understanding. They didn't
20 challenge or provide any evidence that he hadn't had this prior experience.
21 So it all stands un rebutted, all of this evidence. So what have they
22 challenged?

23 I'm watching my timing. Excuse me.

24 They cite nunc pro tunc cases which are not apposite to this situation.
25 Because in the nunc pro tunc cases that they cited, there was no evidence
26 that there was an appreciation at the time that there was this expression. In

1 all of those cases, somebody had to go back and then demonstrate that he
2 could have appreciated, or the Inventor could have had this appreciation at
3 the time because it was there. But his un rebutted testimony that he did know
4 it, he did understand it, he did believe it, and he provided -- we have
5 provided ample evidence to show that it was credible because it was known.

6 I don't know how much of my time I've used of the 10.

7 JUDGE LANE: Go ahead. We had a lot of questions there. I'll let
8 you go on.

9 MR. OLSTEIN: Okay. So now on the diligence question, all right?

10 JUDGE SCHAFER: So let me go back to what the count says. So
11 what he believed at the time, and what you showed later, that you proved
12 later was that what was expressed was 15 contiguous amino acids of your
13 sequence, at least 15 contiguous?

14 MR. OLSTEIN: Well, it was a lot more.

15 JUDGE LANE: Right, right.

16 MR. OLSTEIN: When you look at the sequence comparison --

17 JUDGE SCHAFER: I'm familiar how people right claims.

18 MR. OLSTEIN: Yeah. It was a very long sequence that we actually
19 demonstrated.

20 JUDGE SCHAFER: Okay. And then, also, what about the basis for,
21 when it's administered to a subject, that it would -- induces an antibody or T
22 cell mediate immune response? That's part of the Count Two, particularly
23 that Part B.

24 MR. OLSTEIN: Well, in this case, neither side did any testing at the
25 time, but neither side had challenged that once you knew you had this
26 polypeptide, that it would induce an antibody response.

1 JUDGE SCHAFER: Is the idea that if you put anything that's truly
2 foreign into a body, it's going to --

3 MR. OLSTEIN: Essentially, that's --

4 JUDGE SCHAFER: Yeah, okay. I see your position.

5 MR. OLSTEIN: Yeah. And by the way, we haven't challenged
6 Scarlato's position on that, and they didn't do any testing, either, to show that
7 an antibody was produced. If I may just get a couple of minutes to address
8 the diligence part of our primary case, it goes as follows: Dr. Ruelle did not
9 have a laboratory. He's the Inventor. He came up with the sequence. And
10 so he had to rely on the central laboratory, which Dr. Pullen was the head,
11 was the chief. Dr. Pullen didn't normally do laboratory work, but the
12 testimony that came in, again unchallenged, is that due to prior projects that
13 were present, there was nobody available to do the work. So what did
14 Dr. Pullen do? He volunteered, even though he doesn't normally do bench
15 work, to not delay this project, to start doing some laboratory work. But he
16 also testified, as head of the laboratory, he couldn't devote full time to doing
17 this work because of the fact that he had to attend to his normal duties. And
18 he outlines all these normal duties: lab reports, meetings, outside meetings,
19 et cetera, et cetera, et cetera.

20 So what happens here is he did not work full time on doing the work
21 for Ruelle, the Inventor. We cited two cases that indicate that when you
22 have someone that's not the Inventor doing the work because you have to
23 rely on somebody else, and that you only have to exercise reasonable
24 diligence, that there is some slack. So for example, in the Ray-Bellet (ph.)
25 case that we cited in our Brief, in which they had to send the compounds for
26 testing in another laboratory, there was a long delay in being able to do the

1 work. In the Des Solms v. Schoenwald (ph.) case, 15 U.S.P.Q. 2nd, 1507 --
2 and the Ray-Bellet case, by the way, is 493 F.2d. 1380 -- a graduate student
3 was working, the graduate student could only work part time, and that was
4 considered good enough.

5 So, if you look at the overall work that was done, yes, there are times
6 and periods when Dr. Pullen was working on his normal duties. He
7 effectively was a part-time voluntary person performing lab work. And
8 reasonable diligence doesn't require that he ignore his normal duties because
9 he took on, voluntarily, to do work on this project. And therefore, it's
10 basically our position, and outlined in more details, obviously, in our papers,
11 that there was reasonable diligence considering that Dr. Pullen was part-time
12 working on the project only because he had all these other duties.

13 The only other thing I wanted to add on the diligence aspect, Scarlato
14 argued that Dr. Pullen, when he said he was attending to these other duties,
15 couldn't associate a specific day with a specific duty. That's true, but
16 remember how long ago this was. What Dr. Pullen did testify to, and none
17 of it, again, challenged, is here are my normal work duties, and gave five or
18 six different categories. He then said that I know on those days I was doing
19 one of those duties, but I can't tell you specifically that it was a lab meeting,
20 or an outside meeting, or providing reports that I had to do, or supervising,
21 or helping a laboratory person working on a project, assist them in another
22 project; I couldn't necessarily identify that specifically. But he did identify
23 the type of work and the days on which he did it. And if you go through the
24 diligence chart, you will see all throughout the project, when he started in
25 November, for which we don't have to show diligence, there are always
26

1 periods of time that he was not working on this specific project and
2 attending to other duties.

3 So, the overall pattern is consistent; that basically, because he was
4 head of the laboratory, he could not devote full time to working on the
5 project, and because the other people in his laboratory had already been
6 working on previous projects. So instead of sitting it and putting it aside and
7 waiting until those previous projects were finished, he took up the work, he
8 did it, but he could only do it on a part-time basis because of his other duties.

9 JUDGE SCHAFER: I don't remember from his testimony, did he
10 testify that he worked on it at every opportunity that he had, that he could
11 work on it?

12 MR. OLSTEIN: Basically, yes. I cannot give you an exact quote, but
13 what he basically said, he had to attend to these other duties, he had all of
14 these other duties, and that there was no one else in the laboratory who could
15 do it at the time. And if you look at the pattern, you will see that there are
16 certain times of the month when there's 4 or 5 or 6 or 7 days, whatever it
17 was -- working days I'm talking about -- when he wasn't working on the
18 project but he carefully described all the other duties that he had at the time,
19 and that he was working as best he can.

20 Where does it say that?

21 MR. LILLIE: Right in the last sentence of paragraph 7 of --

22 MR. OLSTEIN: Mr. Lillie pointed out to me, because I didn't
23 remember it by heart, on page 4 of his Declaration, he said, "If I had not
24 been involved in these matters during such period, I would have been able to
25 perform laboratory work on Dr. Ruelle's project, and I would have done so."
26 So I think that answers Your Honor's question.

1 JUDGE TIERNEY: Before we go, I do have a question about the
2 confirmatory testing.

3 MR. OLSTEIN: Yes.

4 JUDGE TIERNEY: And I take it that it's your belief that it was not
5 required in order to get the -- reduction of practice -- in December?

6 MR. OLSTEIN: That it was not --

7 JUDGE TIERNEY: I'm looking at the argument here, and that was --
8 they didn't do the confirmatory test of the expression until a later date.

9 MR. OLSTEIN: That's correct.

10 JUDGE TIERNEY: So at this point, we are -- your actual reduction
11 of practice is based on speculation, however reasonable, that this would
12 actually express in the fashion you say it did?

13 MR. OLSTEIN: I would not call it speculation.

14 JUDGE TIERNEY: But are we certain --

15 MR. OLSTEIN: I would say based on experience --

16 JUDGE TIERNEY: But are we certain to 100 percent that this
17 actually did occur, or are we basically just saying it's reasonable to assume?

18 MR. OLSTEIN: Well, I would say that at the time he was certain to
19 100 percent that the whole group of cells -- now, since you raised the
20 question, if you give me one minute, I'll explain that part of it to you. There
21 is evidence in the record, all right, about clones that didn't work, all right?
22 And Mr. Kreeger, in Scarlato, did cite that work, and that's true. But you
23 have to understand what it means. What we were relying on is a collection
24 of cells. You take a collection of E. coli cells, you transform them with the
25 vector. It may occur that some of the cells do not work and express. And
26 when you isolate a clone, what you're doing is taking a single cell and

1 growing it up and then testing it. So the fact that 1 cell, 2 cells, 5 cells in
2 this whole collection doesn't express doesn't raise an inference that the
3 collection of cells do not express. And from his prior experience in working
4 with it -- and again, at this point, biotech wasn't magic. It was kind of
5 known that if you isolate the DNA, you put it in the vector in the right order
6 so that it's in line with the promoter, you will get that expression.

7 JUDGE TIERNEY: I understand you're saying there's a reasonable
8 belief that expression occurred. But to what extent is it a reasonable belief
9 versus a certainty? Can you address that?

10 MR. OLSTEIN: I don't know if anything is certain in life, but as
11 close as you can be. In other words, the unusual could always happen. At
12 that point, what they're talking about is an unusual occurrence; that if you
13 got zero expression. Is there always a possibility? Yes. But the
14 confirmatory tests show that didn't occur. And I may also point out that a
15 couple of months afterwards, when they did it at the 39 degrees C and took
16 the same vector system, they demonstrated it expressed. It wasn't at the 30
17 degrees C, but it did confirm soon thereafter that the --

18 JUDGE LANE: So when they did the testing in February, they still
19 never did the testing where they were searching for expression at 30
20 degrees?

21 MR. OLSTEIN: That is correct. It was at 39 degrees.

22 JUDGE LANE: So that's what you're relying on for your actual
23 reduction, the practice is expression at 30 degrees?

24 MR. OLSTEIN: That is correct. But what the 39 degree test shows is
25 that the vector was put together right, there wasn't an inherent defect in the
26 vector, that it wasn't something that made it incapable of expressing, that it,

1 you know, it was just a rotten vector or something like that. And it's the
2 confirmatory test -- again, we're not relying on that for his understanding,
3 contemporaneous understanding at the time, it's just to show that his
4 contemporaneous understanding was correct and that his testimony is
5 credible.

6 JUDGE LANE: I understand.

7 MR. OLSTEIN: Thank you.

8 JUDGE LANE: Thank you. Mr. Kreeger?

9 MR. KREEGER: Thank you, Your Honor. These are just exhibits
10 that are already in the record, but I was going to refer to. May I approach?

11 JUDGE LANE: Sure. Mr. Olstein has a copy?

12 MR. KREEGER: He does.

13 JUDGE LANE: Do you have a copy?

14 MR. OLSTEIN: I do. Thank you.

15 MR. KREEGER: I'd like to begin with the Ruelle motion, and I'd just
16 like to point out, for starters, that, although this may be apparent, if the
17 Board agrees with Scarlato on either of our motions, either the Ruelle
18 motion or the Scarlato motion, then Scarlato is entitled to prevail in this
19 case.

20 First, with respect to the Ruelle motion, on the reduction to practice
21 that you've been discussing, the supposed December 1997 experiments, the
22 count in this case is directed to a polypeptide. And there is not data, as
23 Mr. Olstein acknowledged, no data in their notebooks that shows that a
24 polypeptide was expressed in December 1997. So instead, their argument is
25 we constructed the DNA which codes for that polypeptide, inserted it into
26 these E. coli cells, with an experiment design that was set up so that those

1 cells would not express at 30 degrees. That was the point of this suppressor.
2 They were left at 30 degrees until February, at which point they raised it,
3 expressed it, and tested it. So if you look at the entire experimental record,
4 what you see is a set of experiments with a clear experimental design to
5 prevent expression until February, then in February to express. There was
6 never any testing done in the relevant time period of the cells that were
7 maintained at 30 degrees until the interference began in 2009, when they did
8 some experiments.

9 So I think we're in the classic situation here where there's been an
10 attempt to reconstruct a reduction to practice after the fact. We do have
11 Dr. Pullen's bare testimony that he personally believed there was expression
12 at 30 degrees, but there is no contemporaneous document that backs that up,
13 and the experimental design is fundamentally inconsistent with that. If he
14 had that belief, then he should have taken those, and he would have taken,
15 those cells at 30 degrees and had them tested. He simply did not do that.

16 And what's more, to the extent he had that belief, it simply wasn't
17 reasonable. And I'd like to just point out --

18 JUDGE LANE: Mr. Kreeger, let me just -- before you do that, let me
19 see, because I want to make sure I have this straight. Was it at some point,
20 maybe it was in April, the testing was done at 30 degrees to see if some
21 expression would occur?

22 MR. KREEGER: In April 2009.

23 JUDGE LANE: Okay.

24 MR. KREEGER: After the interference began.

25 JUDGE LANE: Okay.

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1 MR. KREEGER: Then, at the direction of counsel, there were some
2 experiments performed.

3 JUDGE LANE: And that did result in expression?

4 MR. KREEGER: Using some very sensitive detection techniques
5 which they didn't have, or weren't even available, and certainly didn't
6 employ, back in 1997, they were able to PCR out, or use very sensitive
7 measures to find some very low levels of expression in 2009. But there is no
8 evidence that that was known at the time.

9 And that's the point I wanted to make, too, Your Honor, is if you look
10 at -- you'll see in Exhibit 20038 we've taken excerpts from Dr. Pullen's own
11 notebook. So there's the cover page. The next page is from the February
12 1998 experiments done with the 39 degrees samples. And actually, there's
13 three different antigens being investigated here. You'll see Orph 1-5 (ph.),
14 Orph 7, and HSF-like (ph.) fragment. The HSF-like fragment is the one
15 that's at issue in this interference. But at the same time that they were testing
16 that antigen, they were also testing vectors that were constructed to express
17 different antigens. And what he did in each case is he made six clones for
18 each of these three antigens and he tested all 18 clones, and all of them had
19 been selected so that they supposedly had the right insert. There was
20 selection process so each one of them had the right insert and was expected
21 to express. And if you look at the results he got, with Orph 1-5, there was
22 no expression, zero for six, and this was after the cells had been raised to 39
23 degrees. For Orph 7, he got one out of six correct. And then if you look at
24 page 51, the next page, that's the HSF-like fragment, which shows that, sure
25 enough, in one out of the six clones, he got expression of the HSF-like
26 fragment at issue in this interference.

1 And we don't contest that they actually got it in February. I mean, we
2 acknowledge that this experiment shown on page 51 demonstrates that they
3 made the protein of the count in February. But what you see here is an
4 experimental design that even when they performed it at 39 degrees as
5 designed, they often did not get expression. In the case of the Orph 1-5, they
6 got no expression. So his subjective belief that, oh, yes, this is leaky and I'm
7 bound to get expression is just simply not true. Even in the experiments
8 done at 39 degrees, they didn't always get expression. Because you can't
9 know until you do the experiment. There was no question about that. All of
10 the experts testified consistently, including the expert for Dr. Ruelle, that
11 until you've done the experiment, you can't know whether you've expressed.
12 So this subjective belief that, oh, yes, I'm sure I've got it, in addition to,
13 frankly, being incredible, is not backed up by the data.

14 I'd like to move on to diligence unless there are further questions
15 about the reduction to practice.

16 So if you look at the diligence chart which Ruelle has submitted, and
17 I've attached it here, that's Exhibit 2064, the relevant time period here is --
18 the critical period starts on January 13th, 1998, just before Scarlato's
19 constructive reduction to practice, and extends up to February 13th, 1998,
20 the date of the reduction to practice. So if you look at the second page of
21 Exhibit 2064, that has the relevant dates, and you'll see that between January
22 13th, '98 and February 13th, '98, that's 31 days of which there are six days
23 that have an actual entry that indicates work on the invention. For the rest of
24 the days, you've got Pullen attended to other work duties, Pullen does
25 laboratory work on another project.

26

1 Now, the law is clear that the entire period had to be accounted for,
2 either with activity or with a legally acceptable excuse. So we clearly do not
3 have the entire period covered with activity, and there's including a two-and-
4 a-half-week period between January 17th and February 4th, which Ruelle, in
5 their brief, acknowledges there was no work done on the invention at all. So
6 we clearly have gaps that have to be explained. And what is the explanation
7 that's been given? All we have is the statements here in this report and in the
8 testimony from Dr. Pullen that he attended to other work duties or worked
9 on other projects. That is the extent of the specificity. And in the Bai vs.
10 Laiko (ph.) case which we cited to, Your Honors, from this Board, it was
11 clear that this kind of either activity or explanations have to be provided with
12 specifics. It can't simply be a vague, oh, I was doing other work. And
13 although he's described these various categories of work, there really is not
14 much more specific than that. He had general duties and he chose to do
15 those instead of this invention. That's just not enough.

16 Now, Ruelle's argument is, well, Dr. Pullen isn't the Inventor, so they're
17 excused, essentially, from showing diligence because Dr. Ruelle handed it
18 off to Dr. Pullen, and then Dr. Pullen, whether he worked on it or not, was
19 sort of out of Ruelle's hands. That's not the legal standard. This isn't the
20 case where an Inventor sent a sample off for testing to some third-party
21 laboratory and was at their mercy. In this case, GSK, the real party interest,
22 employed both Dr. Pullen and Dr. Ruelle. And this is a case like in Bai vs.
23 Laiko, where a single employer has to set priorities. And they clearly set
24 priorities which made this a lower priority project. The testimony from Dr.
25 Pullen was that although he was head of the lab, he had multiple scientists
26

1 and technicians working for him, and he had the option of assigning this
2 project to any of them. He chose not to do that.

3 JUDGE LANE: Well, would it be necessary for diligence for them to
4 drop everything else they're working on and just attend to this?

5 MR. KREEGER: What's required for diligence is that they attend to
6 this project diligently, which means they can't decide as a matter of priorities
7 to attend to a different project rather than this one. That's what the cases
8 say: If they chose to do another invention rather than this one, that's the
9 opposite of diligence. And that was definitely the case here.

10 And I'd just like to point out to one document that kind of confirms
11 that. If you look at Exhibit 2067, this is a contemporaneous memo from
12 December of 1997 that was submitted by Party Ruelle. And you'll see here
13 that, on the very first page, there was a meeting of this group and the mission
14 was to define and implement strategy to identify antigens for otitis media
15 and meningitidis, which is, they were looking for antigens for this particular
16 project. And then -- these pages aren't numbered, so it's going to be a little
17 tricky to show you which page I want to talk about. I want to skip ahead to
18 Addendum 1, which is about five or six pages in. Addendum 1 is a memo to
19 J. Poolman from J. Pullen, Dr. Pullen, their corroborator, which is a
20 summary of the projects that his team is working on. And you'll see that
21 when it comes to neisseria meningitidis, he's got a list of different antigens
22 they're interested in. There's 1.1, 2, 3, 4, 5, 6, 7, 8, 8 different antigens.
23 Each of them is from a different part of the genome, and each of them is a
24 separate project. And then the next page has a list of a Group B neisseria
25 meningitidis vaccine candidates. Do you see that? I want to make sure
26 we're all on the same page.

1 And you'll see there are five listed on the top, Orph 1-2, Orph 3-4,
2 HPUA, LPDB, PILC, those five, then there's a line, then there's three more,
3 Orph 5, Orph 7 and HSF. And again, HSF is the one at interest here. And
4 then if you follow on, there's a detailed description of the first five
5 candidates and what their plans are for them. There's several pages of the
6 first five candidates. And finally, we get to this page which is a landscape
7 page that says "Secondary NMB Vaccine Candidates," that's neisseria
8 meningitis B, and you'll see that HSF is one of the secondary candidates. So
9 if we look at the contemporaneous documents, we see that just as Dr. Pullen
10 testified, they treated this antigen candidate as a promising one, but a
11 secondary one. And that's the way he defined his priorities. Those were the
12 priorities given to him by his employer, and that's the way he set his
13 priorities when it came time to assign work in his laboratory. And this was
14 definitely a low priority project, and the work that was done confirms that.

15 JUDGE SCHAFER: Well, is it your view that it has to be -- to be
16 diligent, it has to be the highest priority?

17 MR. KREEGER: It has to be that -- there has to be either a legally
18 sufficient explanation specifically about what was done instead of this
19 project. And given the fact that there's no specifics, so it's very difficult to
20 evaluate this as opposed to others, and given the evidence that this was not a
21 high priority project, we suggest that's inconsistent with diligence.

22 All right, I'm going to turn to the Scarlato motion unless there's
23 questions.

24 So this is an alternative way for Scarlato to prevail in the case. There
25 actually was a prior conception that comes before the earliest date alleged by
26 Ruelle, and if the Board agrees, then that is a completely alternative way for

1 us to prevail. Because having been the first to reduce as defined by the
2 priority statements and the first to conceive, then Scarlato would prevail,
3 with no showing of diligence being required.

4 So in this case, we have a conception. It was dated August 13th,
5 1997, and we submit that it was definite and firm and permanent because it
6 included the specific sequence at issue. And actually, I might as well turn to
7 that exhibit now. That's Exhibit 1106, the first one in our binder of exhibits.
8 This is a sequence alignment dated August 13th, 1997 that includes a
9 sequence from the meningitidis genome which has been aligned or
10 compared with the HSF protein from an influenza bacteria. And based on
11 this alignment, the Scarlato Inventors realized that they had a protein that
12 was highly likely to be immunogenic because it was highly similar to an
13 immunogenic surface protein expressed in a related influenza bacterium.

14 JUDGE LANE: Mr. Kreeger, before you were talking about this
15 exhibit, how do we know -- or what do we take from that August 13th date?
16 Is that the date this was printed out, is it the date the test was run, and how
17 do we know what that means?

18 MR. KREEGER: Well, it's the date that the analysis was conducted
19 that generated this document. The document was generated on August 13th,
20 1997. That's the testimony of Dr. Pot (ph.). I can't say that the printout was
21 done that day, but the document itself was generated then.

22 JUDGE LANE: And Dr. Pot, he couldn't say as to this particular
23 document?

24 MR. KREEGER: No, but based on the distinctive format of this
25 document and his familiarity with the way these documents were generated,
26 Chiron (ph.), he can say that this document was generated on August 13th,

1 1997 because that's the way the computer systems at Chiron at that time
2 worked. Now, it might have been generated in a file that was since saved on
3 a disk or a hard drive.

4 JUDGE LANE: There was a printout, but --

5 MR. KREEGER: I can't say there was a printout, but eventually it
6 was printed out. The document was generated and the analysis was
7 conducted on August 13th, 1997, based on the distinctive format of the
8 document. I was going to deal with corroboration later, but I will come
9 back to that.

10 JUDGE LANE: Okay. That's fine.

11 MR. KREEGER: But I wanted to first address a point made by Ruelle
12 which we think can be easily dismissed. The claim is that this document,
13 although it includes a specific polypeptide sequence, is not an actual definite
14 and firm conception because the Inventor supposedly could not reasonably
15 have been certain that their sequence was accurate. That's essentially the
16 argument that Ruelle's making, and I think it's just fundamentally
17 misdirected. This is not a question of reduction to practice, this is a question
18 of conception. Did they have a definite and firm idea of a polypeptide
19 within the scope of the count, and --

20 JUDGE LANE: Does the count require that this polypeptide be from
21 the meningitis bacteria?

22 MR. KREEGER: No, what it requires is that -- you've seen the count.
23 There's an alternative. In Alternative B, it requires that the sequence be at
24 least 15 amino acids from the larger sequence and capable of inducing an
25 immune reaction to the larger sequence. Now, it turns out, of course, they
26 were looking for vaccine candidates that were from the meningitis bacteria,

1 and that was certainly their hypothesis, was that this sequence was from
2 meningitis.

3 JUDGE LANE: But so long as you had a sequence that would
4 produce a protein that would induce an immune response, you meet the
5 count?

6 MR. KREEGER: Against the larger. Against the larger. And the
7 testimony is that because of the length of the sequence, it would inherently,
8 necessarily, induce an immune response that would recognize a larger
9 protein of which it was a part. There is no question about that. But as for
10 whether it was part of meningitis, for conception, all they needed was a
11 hypothesis, and that clearly was their hypothesis. Whether they're right or
12 not -- which, by the way, they were -- is part of reduction to practice. I
13 mean, that's where the cases are quite clear.

14 In the cases that -- for example, Burrows Wilcom (ph.), which has a
15 discussion about what it means for the conception to be definite and
16 permanent, make it clear that what's required is that it be specific. The legal
17 standard is that an idea is definite and permanent -- I'm reading here from
18 page 1228 of the Burrows Wilcom case. "An idea is definite and permanent
19 when the Inventor has a specific settled idea, a particular solution to the
20 problem at hand, not just a general goal or research plan he hopes to pursue."
21 And we submit that a polypeptide sequence, it's hard to get more settled and
22 permanent and specific than that.

23 JUDGE TIERNEY: Well, do you want to address what your
24 opponents brought up in the Hintzman vs. Rodderick (ph.) case, a bare hope
25 is insufficient to establish conception?

26 MR. KREEGER: I'm sorry. I just couldn't hear the question.

1 JUDGE TIERNEY: Your opponents pointed out, through the
2 Hintzman case, that a bare hope is insufficient to establish conception. And
3 are we at the level of bare hope here, or are you suggesting that there's
4 more?

5 MR. KREEGER: No, in the Hintzman case, there wasn't a specific
6 sequence, there was a plan, and that's what it was, a hope. This was the sort
7 of research plan type of case. Here we've gotten beyond a hope. I'd submit
8 that the hope was the kind of plan she had when she showed up in
9 Emeryville and began this experimental work. The plan and the specifics
10 comes in the sequence.

11 JUDGE SCHAFER: What's the history of this, of how this paper, this
12 Exhibit 1106, how was it prepared and modeled?

13 MR. KREEGER: All right. Well, actually, this will be helpful. We'll
14 turn to Exhibit 1111, which relates, in part, to this. So the Sand (ph.) case
15 says that contemporaneous documents are the best corroborators, so I want
16 to spend my time, my limited time with you today speaking about the
17 contemporaneous documents. Exhibit 1111 is an e-mail from David Pot,
18 who was at Chiron in Emeryville, where he was outlining what
19 Dr. Massignani's (ph.) project was. She was one of the Inventors. She
20 arrived in Emeryville. She ordinarily worked in Sienna. She came to
21 Emeryville because they had the computing facilities to help her for this
22 project. And it really confirms her plan. It says that she's coming to
23 Emeryville in August, she's going to stay a month, which shows that she did
24 her work in the month of August, 1997; she was going to work with
25 sequences that have been released by the Institute for Genomic Research,
26 and her plan was to look for neisseria meningitidis sequences using

1 bioinformatics techniques to find extracellular molecules that could be used
2 as vaccine candidates, and it goes into the criteria she's going to use,
3 including homology to other known organisms to see if they would be good
4 candidates. And that's exactly what her plan was, that's exactly how she
5 testified to her plan, and it confirms both the date and the existence of the
6 plan.

7 Then we have Exhibit 1106 itself, and the testimony here is that
8 Dr. Masignani says she generated it on August 13th, 1997.

9 JUDGE SCHAFER: How was that? Give me some details. How was
10 it generated?

11 MR. KREEGER: Oh, okay. So this now, we're talking, you know,
12 her testimony. She said she had a series of sequences that had been released
13 by this TIGR, it's referred to, The Institute of Genomic Research, and she
14 began searching them and began to find homologies between those
15 fragments with other organisms, and eventually, she -- and if she could, she
16 tried to stitch them together to create longer contigs or longer sequences that
17 might be more useful, and eventually, she found this one, and others. She
18 had about ten candidates, I think she testified to, that were strong candidates.
19 And this one, once she realized that it could be -- two different sequences
20 could be joined to create the longer sequence, and that that longer sequence
21 had a high degree of homology to this influenza surface protein, she
22 identified it as a very strong candidate for further research, and that's what
23 the printout -- was the basis for the conclusion.

24 JUDGE SCHAFER: Well, how was the printout made? I'm still --
25 she was piecing things together, but how do we get to that, the printout from
26

1 that? Did she grab certain data and say, oh, here, please put these together
2 for me?

3 MR. KREEGER: No, she did the work herself. She did it on a
4 computer, and she took the sequences and aligned them and joined them to
5 create the longer contig. She named that longer contig GNMAA-84R. So
6 this is an alignment between GNMAA-84R and the HSF sequence, which
7 was in a publicly available database. Although it was posted on Chiron's
8 servers, it was a public database similar to, you know, the kind of
9 depositories people do when they run blast searches today. And she
10 basically blasted the GNMAA-84R against all known sequences out there
11 and discovered this homology.

12 JUDGE SCHAFER: Okay. So she puts the things together and says
13 now go search for this and see what's close?

14 MR. KREEGER: Yes.

15 JUDGE SCHAFER: That's what's going on. Okay.

16 MR. KREEGER: Exactly. So what we have here -- and then we have
17 Dr. Pot's testimony that goes through in detail about the distinctive qualities
18 of this printout and how consistent it was with the way the Chiron system
19 worked that further establishes the authenticity. The date shows that it was
20 made in the relevant time period when she was known to be at Emeryville.
21 And he remembers setting up a special directory for her to work, which is --
22 you'll see it on the printout, it says Z3/U1/PotD -- that was his name --
23 /Vega. That's Dr. Massignani's first name. That was the directory he set up
24 for her specifically to record her, the results of her work.

25 So under the rule of reason, you're supposed to ask does this all hang
26 together, does it make sense? And we submit that it does; that the

1 independent non-Inventor testimony confirms and is completely consistent
2 with the story that this was the time when she was doing her work, this is a
3 printout that shows that it was made from Chiron in Emeryville, it's
4 consistent with her story, and corroborated. I would also point out the
5 several cases that establish that physical evidence such as this document,
6 1106 and 1111, are the best forms of corroboration of Inventor testimony.

7 Finally, I want to address this point about the -- after they left
8 Emeryville, they made a slight change to the sequence. They deleted a
9 particular nucleotide which had the effect of extending the reading frame
10 even longer. So this is one nucleotide change. And our opponents make a
11 big fuss about this in saying that it somehow undermines the definiteness or
12 the completeness of the conception, and that, again, completely
13 misunderstands the legal standard. This particular sequence was conceived,
14 and it's within the scope of the count. A later sequence that is even larger
15 was conceived at the time they filed the patent application, and that's also
16 within the scope of the count. The fact that they made that change doesn't
17 say that there was constant flux. Just the opposite; it's a very minor change
18 that actually had the effect of making an even larger protein that was within
19 the scope of the count. But both of them are completely conceived at the
20 relevant time period.

21 And I guess I'd like to reserve the remainder of my time to respond to
22 Ruelle, unless there are further questions.

23 JUDGE LANE: Thank you.

24 MR. KREEGER: Thanks.

25 JUDGE LANE: Mr. Olstein?

26

1 MR. OLSTEIN: Just a moment of time to respond to our priority
2 case. One, on the diligence, the arithmetic that was presented by Scarlato is
3 a little wrong because he left out the weekends. So it's really 6 out of 23, not
4 6 out of 31. So that's number one. And we've already set out our position
5 that the cases he cited were standards for the Inventor, not standards for
6 someone doing work on behalf of the Inventor, of accounting in detail for
7 every day. The two cases that I cited in the beginning, and then in the Brief,
8 shows that when someone else is doing the work and they have other duties
9 and there are delays in doing it, those are considered to be excused for the
10 purposes --

11 JUDGE LANE: Is there a different standard when they're both
12 working for the same person? Like Mr. Kreeger was saying, it's not like the
13 situation where you send something out for testing at an outside laboratory
14 that --

15 MR. OLSTEIN: In both -- I'm sorry, Your Honor.

16 JUDGE LANE: Go ahead.

17 MR. OLSTEIN: In both of those cases it was internal. In one, it was
18 graduate students working in the laboratory of the Inventor who were part-
19 time students. In the other one, it was a large pharmaceutical company in
20 which the laboratory, from doing all the testing of the compounds, was
21 backed up. They had a shortage of test animals in that case rather than a
22 shortage of people, and they weren't able to get to the testing.

23 The other thing I want to address is, again, just briefly, to remind the
24 Court that non-working parts in Dr. Pullen's notebook were clones, single
25 cells of the entire collection. And the testimony that was given by the
26 expert, when asked in cross-examination, the questions were directed to

1 clones, not to the entire population of clones. And when they said, yes, at
2 times we find clones or individual cells that are not expressing, that is not an
3 admission or testimony that when you have a collection of cells, that you
4 wouldn't have expected it to express once you had experience with the
5 vector and the expression system.

6 JUDGE SCHAFER: So that first set where it was held at 30 degrees,
7 the first set, the first test or the first experiment and it was at 30 degrees, that
8 was a collection, that wasn't separate clones?

9 MR. OLSTEIN: That's correct.

10 JUDGE SCHAFER: And then when you repeated it and did the
11 confirmatory test in 2009, that again was done on the collection?

12 MR. OLSTEIN: It was done on a clone from the collection. But
13 you've got to remember, if a part of the whole is expressing, then the whole
14 is expressing.

15 JUDGE SCHAFER: Okay. So what you're saying is that when
16 cloned, that -- from what he was saying, there was one clone that did
17 express?

18 MR. OLSTEIN: And five that didn't.

19 JUDGE SCHAFER: And five that didn't. And what you're saying is,
20 that particular clone was in the earlier test?

21 MR. OLSTEIN: The six -- you've got to remember that there was --

22 JUDGE SCHAFER: Yeah, there were six, and you had a collection.
23 And I take it's the collection --

24 MR. OLSTEIN: There's hundreds of thousands of cells in the
25 collection.

26 JUDGE SCHAFER: Right.

1 MR. OLSTEIN: You take six cells out of the collection, out of the
2 hundreds of thousands, and that's called a single cell, and then you grow up
3 that single cell into a multiplicity of the same cell.

4 JUDGE SCHAFER: Okay, my question goes to how do you know
5 that particular cell that you used later was also the same identical type cell
6 that was in the collection earlier?

7 MR. OLSTEIN: Because it is the same -- it was saved. In other
8 words, if you read our evidence, it was in a refrigerator, there was a whole
9 line of testimony that it's the same one, had Pullen's name, dates, and all the
10 rest of that.

11 JUDGE SCHAFER: I see. Okay. And then certain ones were
12 selected out of that, and at least one of them --

13 MR. OLSTEIN: Was saved.

14 JUDGE SCHAFER: -- expressed?

15 MR. OLSTEIN: Yeah. But the fact that those five individual cells
16 didn't express doesn't have anything to do -- it's a red herring.

17 JUDGE SCHAFER: Yeah, I understand that. I'm just trying to make
18 sure that I understand.

19 MR. OLSTEIN: No, what was saved was the working clone. That
20 was saved.

21 JUDGE SCHAFER: What was saved was the collection, and the --

22 MR. OLSTEIN: No, not the collection, the working -- the clone that
23 was tested that was part of the collection was saved, not all of the cells.

24 JUDGE SCHAFER: Okay. So it was removed from the collection
25 early on and saved?

26 MR. OLSTEIN: Correct. And tested in February.

1 JUDGE SCHAFER: Okay.

2 MR. OLSTEIN: And then it was saved.

3 JUDGE SCHAFER: And then that same one was tested again at 30
4 degrees, later?

5 MR. OLSTEIN: In 2009.

6 JUDGE SCHAFER: Yeah.

7 MR. OLSTEIN: So it's the same -- it came out of the collection, all
8 right? It was multiple cells, because you take a single cell and you grow it
9 up into multiple cells. But that was a sample that was saved from the
10 original, and there's a -- it hasn't been challenged by Scarlato, the history and
11 the evidence. You know, we traced it through the label. There was
12 testimony of the person that put it in, that got it back out. So that is not
13 challenged by Scarlato.

14 JUDGE LANE: Is the testimony such that we could conclude that
15 everything was done exactly the same way in April of 2009?

16 MR. OLSTEIN: Yes. And that, again, wasn't challenged by Scarlato.
17 If he thought that it wasn't done in the same way, he had an opportunity to
18 comment on it and to --

19 JUDGE SCHAFER: No, what Judge Lane's getting at is when you
20 move for benefit, you have the burden separate from a challenge or not.
21 Even if they had decided to not show up at all, you still have the burden to
22 prove your case.

23 MR. OLSTEIN: And our Declaration --

24 JUDGE SCHAFER: I mean, so that's what the question goes to:
25 Were the things identically done so we feel confident that they reflect what
26 existed earlier?

1 MR. OLSTEIN: And the answer to that question is the expression
2 was performed in the same way, under the same conditions, and that's what
3 the Declarations say. You can read the conditions and compare it one to the
4 other. They were the same. So I agree it's our burden of proof, I'm just
5 making the point that it wasn't challenged. And I would assume if there
6 were holes and there were differences, that Scarlato would have raised that
7 immediately.

8 So now, if I may go on to Scarlato's case, in Exhibit 1106, which I
9 hope Your Honors still have, I think there's a fundamental misunderstanding
10 of what 1106 is. And I would like to start off by saying what 1106
11 demonstrates is what I would call computer conception. The computer
12 conceived something. What do I mean? And it doesn't show that the
13 Inventors had and understood what was done.

14 So what happens? If you look at Exhibit 1106, they start out with a
15 polynucleotide. We don't know where that came from because -- except
16 from the Inventor's testimony, uncorroborated. That polypeptide is taken
17 by -- polynucleotide is then taken by the computer and translated into
18 polypeptide. And what happens there, there's six frames so there's six
19 possible polypeptides. Then what the computer does is then ran a search
20 automatically of the polypeptides that were created from that polynucleotide,
21 again unidentified, and came up with one of the polypeptides that had a high
22 homology to the HSF protein that you see in 1106. Now, the dates and the
23 times that are shown in here, as Dr. Pot testified in his Declaration, and as
24 we pointed to, merely shows when the computer made the calculation. So if
25 you look at the second line, on Wednesday, August 13th, 9:56 was when the
26 computer did the translation, as I said, of the polynucleotide into polypeptide

1 sequence. At 10:09 on August 13th, the computer now did a homology
2 search, completed it, and came up, apparently with the sequence comparison
3 of the GNMAA to the HSF protein.

4 JUDGE LANE: But the computer was doing what it was told to do.

5 MR. OLSTEIN: That is correct.

6 JUDGE LANE: Right. I mean, someone had to --

7 MR. OLSTEIN: Told it to make a query on the polynucleotide.
8 Someone pressed a button. But I'll get back to what it was, but my point
9 here at this point is, all this indicates is that deep on a hard drive in the
10 computer, this information is recorded. But it doesn't show and doesn't tell
11 anyone when the Inventor saw it. So if I do a computer calculation that gets
12 put into the hard drive, it doesn't mean that this was printed out, that the
13 Inventor ever looked at it, ever appreciated what the sequence was, ever saw
14 the sequence, or ever saw the comparison. All this piece of paper does by
15 itself is show that somewhere in the computer this information was stored
16 and the time when it was stored. There's no conflict in that testimony. If
17 you read Dr. Pot's Declaration, that's clearly what he says. Now, how --

18 JUDGE LANE: Well, is it reasonable to think that the Inventor went
19 down for this specific purpose, to run this type of test, and then would not
20 have looked at the data generated?

21 MR. OLSTEIN: Well, now you have to understand what the overall
22 testimony was. TIGR had a database. And I'm not going to go in right now,
23 because I don't have the time, is there faults in that database and the
24 sequence accuracy, and all the rest. That's all in our Brief. But there are
25 2,000 fragments in there. And what Dr. Massignani was doing was typing in
26 computer instructions, take these 2,000 sequences, rearrange them, do this,

1 do that, and the computer's recording each time it does something, all right,
2 and maybe do sequence comparisons. So I don't know how many
3 comparisons were done. She said in her Declaration they were using the
4 entire TIGR database of 2,000 fragments. So, yes, looking at this
5 individually stored in the file, this is a single piece of paper, but it could
6 have been among thousands of recorded things. Because they were doing
7 what I call shotgun searching of shotgun sequences. By shotgun sequences,
8 randomly sequenced. They were doing random searches. And it's their
9 burden to show when the Inventor first had an appreciation of the sequence,
10 knew it and understood it.

11 Now, of course, Dr. Masignani and another Inventor said, oh, we
12 looked at it sometime in August, but that's not corroborated. Unlike the
13 laboratory notebooks that Scarlato refers to, in that case you have an
14 Inventor putting sequence down in a laboratory notebook, so you know the
15 Inventor knew what was there at that date, et cetera, et cetera. But when
16 something is in a computer file along with who knows how many other
17 sequences and how many other searches that were done, it's their burden to
18 show when the Inventor first had knowledge of that sequence, and there is
19 nothing of record except this printout. This printout is just a hard copy of
20 something stored in a computer file.

21 JUDGE SCHAFER: Do you have any doubt that this data existed on
22 the date August 13th?

23 MR. OLSTEIN: I have no way to -- I do not doubt because I have no
24 way to challenge --

25 JUDGE SCHAFER: Whether or not --

26

1 MR. OLSTEIN: Unless I went and grabbed the hard drive and found
2 that it wasn't there, I have no way.

3 JUDGE SCHAFER: Right. Your position is we don't know when the
4 Inventor knew this.

5 MR. OLSTEIN: That's correct.

6 JUDGE SCHAFER: But you don't have any doubt that on
7 August 13th of '97, that this particular bit of data existed in the form that's
8 shown here?

9 MR. OLSTEIN: In the computer? I have no way to challenge that. I
10 have no reason to challenge that it existed on a hard drive, or whatever it's
11 called. I'm not a computer expert, but somewhere in some file, it existed.

12 Now, so, what we're depending on is uncorroborated testimony of the
13 Inventor that she saw this prior to our conception date. We don't know that
14 because there's nothing on this that has any date of when this was printed
15 out, that verifies when it was first available to the knowledge of the Inventor,
16 this sequence. So that's what I meant by computer conception. The
17 computer saw it. The computer, maybe, appreciated it. But I don't know
18 from this record when the Inventors first appreciated it, and all we have is
19 their uncorroborated testimony that they saw it. And again, as I said, it's not
20 a single thing that was being done. There were thousands of sequences that
21 were being looked at by pushing --

22 JUDGE LANE: What's your evidence that thousands of sequences
23 were being looked at?

24 MR. OLSTEIN: Because they said that they downloaded the 2,000-
25 and-some-odd sequences from the TIGR database, which is the meningitidis
26 database, into their database to then assemble and do comparisons. And the

1 general testimony, okay -- and I'll go into the specific corroboration by Pot
2 and the other people -- was that this was a gigantic project; they were going
3 to search through the entire database, starting to look for sequences in that
4 database that had homology to known sequences, and then out of those
5 known sequence -- then look and see from those known sequences whether
6 those sequences met a certain category which were either virulent sequences,
7 a certain type of leader or peptide sequences, and then out of that, go out and
8 select certain sequences for further looking, for further investigation. So by
9 their own testimony, there were thousands and thousands of sequences
10 sitting in this computer, they were all being compared and being searched
11 into the database for homology, so it's their burden to show when the
12 Inventor first appreciated it.

13 JUDGE SCHAFER: Is there any doubt in your mind or any reason
14 why we shouldn't believe that Dr. Massignani -- and I'm talking about Exhibit
15 1106.

16 MR. OLSTEIN: Yes.

17 JUDGE SCHAFER: Put in the sequence into the computer that's
18 here? I guess it's the GNMAA-8, it looks like.

19 MR. OLSTEIN: Well, she said that's what she did, but then again, if
20 you read our Brief and you read her deposition testimony, which we did, her
21 memory of what she did is so vague. She testified there were four or five
22 different things that were done. So for all I know, she didn't enter the
23 GNMAA-84R; that that, again, was created by the computer based on the
24 TIGR database, searching the TIGR database in order to put the contigs. It's
25 not a question that she necessarily put the two fragments together to make a
26 longer fragment and then independently went and did the search. That's

1 what she said she did, but then she said she did a lot of other things. But
2 again, all of that is uncorroborated.

3 JUDGE SCHAFER: So is your position this was -- they just had a
4 computer program that looked for stuff and threw it all together, and then
5 came up with just thousands of possible reports?

6 MR. OLSTEIN: And then those reports would have been examined.

7 JUDGE SCHAFER: How's that different from what everybody else
8 in biotech does?

9 MR. OLSTEIN: Well --

10 JUDGE SCHAFER: Isn't that what you all do? I mean, when you get
11 down to it, you have these sequences out there and you're looking for
12 matches and --

13 MR. OLSTEIN: Well, that is correct. But the difference is --

14 JUDGE SCHAFER: So nobody's inventing?

15 MR. OLSTEIN: No, that's not what -- no.

16 JUDGE SCHAFER: I mean, it seems to me that that's how the
17 invention seems to work in the biotech area.

18 MR. OLSTEIN: But, you see, our point is not that. Our point is, is
19 what happened in Ruelle's case, he did do that search. But then there's a
20 documented time and date when he printed it out. There's a documented
21 time -- when I say time, date, not the time -- when he handed that sequence
22 off to someone in their laboratory notebook, so you know exactly -- what we
23 have here, I said, is a document which, by their own testimony, just says
24 when the computer file was created. Everything else is Inventor testimony.

25 Now, I know they talk about the Corroboration Declarations, but the
26 Corroboration Declaration says we know that she was going into the TIGR

1 database with these couple of thousands fragments, or shotgun sequences as
2 they're called, and she was going to try to piece them together and try to look
3 for homology searches and do that, but that's general. It doesn't show this
4 was seen by the Inventor. It doesn't show -- I mean, if you just look at this
5 document by itself, which is the corroboration document, all that shows it
6 was stored in a file -- that's a so-called Vega file in Massignani's file -- it
7 doesn't show who actually entered the sequence or where it came from,
8 assuming that that entire sequence was entered. I know she said she did, but
9 that's uncorroborated. So what we really have here is a document that's so
10 indefinite that it doesn't establish a date. It was their burden. The only date
11 they've asserted is August 13th. That's the conception date they've asserted.
12 They haven't attempted to prove any other date. And all this shows, at best,
13 is there was a file in the computer that had this sequence.

14 JUDGE LANE: Now, Mr. Olstein, you want to wrap up?

15 MR. OLSTEIN: Yeah. Just want to touch briefly on -- the other
16 parts, I'll rely on the Brief, because Dr. Dyer explains why. And I want to
17 point out that a question was asked whether the count required it to be a
18 meningitidis sequence. If you will look at Scarlato Fact 76, they clearly and
19 unequivocally say in their fact that the immunogenic fragment of the count
20 is a native protein fragment, and they define it as a native protein as a
21 Men-B (ph.)protein. So, on this record --

22 JUDGE LANE: But it is, right? I mean, we know that to be the case
23 now?

24 MR. OLSTEIN: Yes, but what they're -- yes, we do. But saying that
25 it -- the whole idea of this thing, it can't be something that's random. In
26 order to have a permanent idea of something -- and we explained why, from

1 the database, you'd have no reason to believe that this is a real sequence, and
2 that's the -- I'm going to rely on the Brief because I'm out of time. The only
3 last thing is the state of flux. What Scarlato alleges is a small change, it's not
4 a small change. And what has to be the definite permanent in the Inventor's
5 mind -- at some point they must have seen this sequence, but they weren't
6 yet satisfied with that sequence because, as I said, the computer generated
7 this, now we have the hand of man, right? What does the hand of man do?
8 It looks at this thing and says, I'm not so sure this sequence is correct. Yes,
9 they only found one error, as they said, which is a major error; significantly
10 changed the protein. It's all in our Brief. But they could have found 20
11 errors. And until they ran that analysis to look at it and find out whether this
12 was a good sequence or a bad sequence, all they had was a
13 computer-generated sequence, no intervention by the hand of man.

14 It's only when it came out and was evaluated -- because as Judge
15 Schafer said, what is the Inventor, you know, the human part of this? Well,
16 it's looking at the sequence, evaluating the sequence, deciding whether it's
17 correct or not, what its use is, and what its purpose is. The computer didn't
18 do that. They did it at some time. I don't know when they saw it. And they
19 clearly knew they had to look at it and evaluate it, and when they did, they
20 found an error. It's a frame shift. It's deleting something; changed numerous
21 amino acids at the front part. So the invention wasn't complete until they
22 looked at it, evaluated it, and made whatever changes they needed to make.

23 JUDGE LANE: All right. Thank you.

24 MR. OLSTEIN: No further questions, I will sit.

25 JUDGE LANE: Thank you. Mr. Kreeger?

26

1 MR. KREEGER: Let me just take that last point first. On the
2 definiteness, the Burrows Wilcom case has this comment that if an idea is in
3 constant flux, conception is not complete. But the very next sentence of the
4 opinion says "A conception is not complete if a subsequent course of
5 experimentation, especially experimental failures, reveals uncertainty that so
6 undermines the specificity of the Inventor's idea, that it is not yet a definite
7 and permanent reflection of the complete invention." And what we have
8 here is a specific idea. The fact that they improved on it and created a longer
9 sequence doesn't undermine the specificity of it as it existed in August.

10 Now, on the corroboration point on this Exhibit, the rule of reason
11 says you don't throw out the Inventor's testimony entirely, what you do is
12 you ask does the other evidence coming from someone other than the
13 Inventor corroborate their story, does it makes sense. In this case, we have
14 Dr. Massignani say that she generated the GNMAA-84R sequence. Does that
15 make sense? Well, Dr. Pot says that's exactly what she was there to do in a
16 contemporaneous e-mail and his testimony. She took that sequence, she ran
17 this alignment. There's no question that the alignment was run in August.
18 She says she printed it out then, in Emeryville. She looked it over with Dr.
19 Rappuolli when he visited Emeryville in August. That's her testimony.
20 Does the document, you know, on its face, unequivocally establish the date
21 she printed it out? No. Is it consistent with her testimony of that's when she
22 printed it out? Absolutely. It has her handwriting on the top of the printout,
23 which says, in Italian -- we had a translation, I think it's in the record -- "Not
24 in NG," not in gonorrhea.

25 So this was a sequence that she had discovered, not only that it was
26 present in meningitidis, but it wasn't present in another organism, gonorrhea.

1 She evaluated the sequence at the time, that's her testimony, and I think the
2 overall evidence, taken as a whole, corroborates that testimony. The rule of
3 reason doesn't require that every specific act be corroborated in the sense
4 that there's a document or an over-the-shoulder observer that's established.
5 You have to ask, on the whole, is this a fraud or is it genuine? And we
6 submit that the evidence shows this is not a fraud.

7 On the point of thousands of alignments, there's no testimony to that
8 effect. The testimony is that she did many different searches, but when --
9 she found a small set that she was convinced were strong candidates, and
10 this was one of them. She didn't remember the exact -- I think -- I'm going
11 to from memory here. It's approximately ten candidates that she brought
12 back from Emeryville to Italy as the ones they wanted to pursue, and this
13 was one of them. Does that testimony --

14 JUDGE LANE: So would she have generated a computer file, or
15 whatever this is, like this for thousands of different sequences?

16 MR. KREEGER: There's no testimony to that effect. I don't think she
17 was asked, and I don't recall any testimony as to how many computer files
18 like this existed at the time. What she said was she printed out the ones that
19 she was interested in, and it was a relatively small set, and this was among
20 them. That was her testimony, and I think the document is consistent with
21 that.

22 JUDGE SCHAFER: So she would have been looking for a lot of
23 things simultaneously?

24 MR. KREEGER: Sure.

25 JUDGE SCHAFER: Which, I think, is what you all do.

26

1 MR. KREEGER: Absolutely. She had a series of criteria, and they're
2 spelled out in her Declaration and the other corroborators' Declarations of
3 how she was going to evaluate these sequences. And one of the key criteria
4 was does it align with a surface-expressed protein that's immunogenic in a
5 related organism? And that's why this was such a valuable hit, because it
6 did.

7 Lastly, I just want to spend a minute on the Ruelle motion. The claim
8 about these clones, I just want to make sure the record is clear here. There
9 were multiple clones that --

10 MR. OLSTEIN: Your Honor, I think now he's doing a rebuttal of my
11 rebuttal.

12 JUDGE LANE: I'm sorry.

13 MR. OLSTEIN: I apologize.

14 JUDGE LANE: Yeah, let me -- I didn't follow how -- you jumped up
15 before I was quite following your point. So go ahead, Mr. Kreeger, let --

16 MR. KREEGER: If the Board will hear me, I'd like to just address
17 briefly the Ruelle motion for my last statement.

18 JUDGE LANE: Okay. Okay.

19 Do you think that's okay? All right. Just --

20 MR. KREEGER: I just want to make sure the record is clear about
21 this clone point, okay?

22 JUDGE LANE: Go ahead. Go ahead.

23 MR. KREEGER: There were a series of cells, E. coli cells, and as I
24 pointed out in Exhibit 2038, they were working with three different antigens,
25 three different vectors. Those vectors were introduced into E. coli cells, and
26 then they took multiple clones out. The claim was that they are certain that

1 it will always express. Maybe a particular clone won't, but they are certain
2 that it will express somehow, and that is just not consistent with the record.
3 Because when it came to the Orph 1-5 antigen, they did not express at all, in
4 any of the clones. And there's a contemporaneous document --

5 Is that 2069?

6 MR. LITTLEFIELD: 2069.

7 MR. KREEGER: 2069. I don't have it here, but there was a
8 document contemporaneous from the time that concluded they did not
9 achieve expression of the Orph 1-5 antigen. And they knew that because
10 they actually did testing. So the claim now that, oh, we knew we were going
11 to express the HSF protein, that is classic hindsight, nunc pro tunc thinking
12 because they couldn't know until they did the tests. And that's what the
13 Orph 1-5 data shows. And with that, I'll submit.

14 JUDGE LANE: Thank you. Did you want to say something quick in
15 rebuttal to that, Mr. Olstein?

16 MR. OLSTEIN: I'll say just two things in rebuttal. On the Scarlato
17 motion, he talks about the examination, et cetera, et cetera. My question --
18 and the printout and the handwriting, it's when. I'll say it again --

19 JUDGE LANE: I guess I was getting at did you want to say anything
20 about what Mr. Kreeger just said about the cells?

21 MR. OLSTEIN: Yes, I do, because, again, a clone is a clone is a
22 clone. The fact that the four or five clones that were grown out of the
23 literally hundreds of thousands of cells didn't express just means -- it doesn't
24 indicate that there wasn't expression from the collection of cells, it's just that
25 at that point, they selected clones that didn't work.

26 JUDGE LANE: All right. Thank you.

1 (Whereupon, the proceedings, at 2:30 p.m., were concluded.)

2

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